REMARKS

Status of the Claims

Claims 3-8, 12, 13, 15-17, and 19-23 are pending in the application.

Traversal of restriction requirement

Applicants maintain their traversal arguments pertaining to the restriction requirement, filed in the response of September 20, 2001, and preserve their right to petition the Commissioner to review the requirement. In accordance with MPEP 818.03(c), the petition may be deferred until after allowance of claims to the elected invention, or an appeal is filed.

Rejection of the Claims Under 35 U.S.C. §103(a)

Claims 3-8, 12, 13, 15-17, and 19-23 stand rejected for allegedly being obvious over the abstracts of Neuman and Guenther. Applicants respectfully traverse for the reasons discussed below.

Neumann discloses that an estrogen-progestagen combination can be used for treating certain disorders such as premenstrual syndrome (PMS). Also, Neumann does not make reference to any particular species of estrogen or progestagen. Guenther discloses a transdermal formulation for treating PMS which includes a single species of progestagen (gestodene) optionally in combination with estrogen.

Neither Neumann or Guenther discloses a method for treating patients suffering from premenstrual dysphoric disorder (PMDD) using a combination of estrogen and progestagen. More importantly, practitioners and researchers in the field of obstetrics and gynecology clearly recognize that PMS and PMDD are distinct clinical disorders (see e.g, the attached review of a roundtable discussion of practitioners in women' health which opines that PMDD is a distinct clincal disorder) with different characteristics and treatment approaches(see e.g., Steiner et al. (2000) *International Clinical Psychopharmacology* 15 (suppl 3): S5-S17). Steiner provides a detailed summary of the characteristics of the two disorders noting that women with PMDD do not respond to conservative and conventional interventions, page S7, first column).

PMS is typically treated with a non-pharmacologic treatment approach including lifestyle changes, stress management, diet, exercise, and cognitive/behavioral therapy. The sufferers of PMDD can often have symptoms severe enough that social and occupational functioning are impaired. PMDD sufferers are often treated with a pharmacologic treatment approach which may include gonadal hormone supression and serotonergic antidepressants (see e.g., Steiner and Born (2000) *International Clinical Psychopharmacology*, 15 (suppl.3):S5-S17). Additionally, investigators in the field of premenstrual disorders have attempted to make further refinements in rating scales which can be used in the classification and diagnosis of these different premenstrual disorders (Steiner et al. (1999) *Journal of Affective Disorders*, 53: 269-273).

In the recent roundtable discussion of experts, a consensus was reached that there is sufficient evidence to support the notion that PMDD is a distinct clinical entity which is distinguishable from PMS. Practioners and researchers now routinely recognize that functional impairment is a unique characteristic of PMDD. Also, it is frequently the case that PMS responds to a non-pharmacologic treatment approach while PMDD sufferers respond to a pharmacologic treatment approach. In one clinical trial, fluoxetine was screened for treating PMDD sufferers (see e.g, Steiner et al. (1995) *New Eng. J. Medicine*, vol.332, no.23, pages 1529-1534).

Further in support of the notable differences between PMS and PMDD, an attached 132 Declaration, provided by Dr.Sampson-Landers and Dr. Foegh, provides a summary and characterization of the distinctions between PMS and PMDD . At page 3 of the 132 Declaration, Table 1 summarizes the major distinguishing features between the two disorders.

Applicant's invention is related to a method for treating PMDD using a therapeutic gestagen in combination with estrogen In view of the distinct clinical differences between PMS and PMDD, it would not be obvious to one of ordinary skill in the art that a therapeutic agent that would be efficacious for PMS would have similar efficacy of PMDD. As summarized in the 132 Declaration, based on the multitude of differences in particular the treatment approaches between PMS and PMDD, it would not be apparent to one of ordinary skill in the art from reading the disclosures of Neumann or Guenther that the gestagen/estrogen combinations would have utility for treating the distinct clinical disorder, PMDD.

A mere "obvious to try" is not a sufficient basis for a valid test of patentability, *In re Dow Chemical Co.* (CAFC 1988) 837 F.2d 469, 5 PQ2d 1529. The argument as posited by the Examiner is of the "obvious to try" type and as such is not a sufficient legal basis for a rejection based on obviousness. By the mere disclosure that PMS is treatable with an estrogen or a progestagen would not lead one of skill in the art to combining a gestagen with an estrogen for treating women suffering from the unrelated PMDD. Therefore, the rejection of the pending claims under §103 of the patent statute should be withdrawn.

The literature references discussed herein are not submitted in an Information Disclosure Statement as the references are not relevant to patentability of the instant invention.

Favorable action on the application is earnestly solicited. The Examiner is kindly invited to contact the undersigned by telephone to discuss matters which may further the prosecution of this application or facilitate the allowability of some or all of the claims.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version With Markings To Show Changes Made".

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

Robert E. McCarthy, Reg. No. 46,044
Representative Capacity

Harry B. Shubin, Reg. No. 32,004
Attorney for Applicants
MILLEN, WHITE, ZELANO & BRANIGAN, P. C.
2200 Clarendon Boulevard, Suite 1400
Arlington, Virginia 22201
Direct Dial: (703) 812-5322
Internet address: mccarthy@mwzb.com

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Please amend claim 3 as follows:

3. (Twice Amended) A method of treating premenstrual dysphoric disorder comprising administering to a patient in need of such treatment a therapeutically effective amount of gestagen ~~The method of claim 1~~, further comprising ~~administering~~ an estrogen.